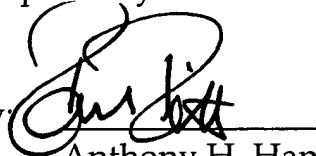


REMARKS

The claim amendments are made in order to remove multiple dependencies.

Respectfully submitted,

By


Anthony H. Handal
Reg. No. 26,275
Roger Pitt
Reg. No. 46,996

Express Mail Label No. EL695230229US

1. (amended) A method of diagnosis of onset of endotoxemia or sepsis due to Gram negative bacterial infection said method comprising monitoring of the degree of AP occupancy of LPS (Lipopolysaccharide) binding sites on alkaline phosphatase in a sample of tissue or fluid derived from a patient, wherein the degree of AP (Alkaline Phosphatase) occupancy is associated with presence or absence of Gram negative bacterial infection.

3. (amended) A method according to claim 1 ~~or 2~~, wherein the degree of AP occupancy of LPS binding sites on alkaline phosphatase in a sample or tissue or fluid derived from a patient, is monitored over a period of time, wherein a decline of the degree of AP occupancy indicates Gram negative bacterial infection.

4. (amended) A method according to ~~any of the preceding claims~~ claim 1, wherein the degree of AP occupancy of LPS binding sites on alkaline phosphatase in the sample is determined and wherein onset of decline in the degree of AP occupancy indicates onset of Gram negative bacterial infection.

5. (amended) A method according to ~~any of the preceding claims~~ claim 1 wherein the degree of AP occupancy of LPS binding sites on alkaline phosphatase may also indicate a mixed or single infection of Gram negative and Gram positive bacteria.

6. (amended) A method according to ~~any of the preceding claims~~ claim 1 wherein the sample is subjected to binding with a ligand for the LPS binding site on alkaline phosphatase followed by a determination of the degree of binding of the ligand.

7. (amended) A method according to ~~any of the preceding claims~~ claim 1 wherein the ligand for the LPS binding site on alkaline phosphatase is selected from the group consisting of naturally occurring ligands, chemically modified or genetically modified derivatives of natural LPS binding site binding substances, chemically produced ligands.

8. (amended) A method according to ~~any of the preceding claims~~ claim 1, wherein the sample is subjected to binding with a ligand for the LPS binding site on alkaline phosphatase selected from LPS, Lipid A, and LPS binding site antibody against alkaline phosphatase, a Fab fragment with LPS binding site binding ability on alkaline phosphatase, a single chain fragment of an

immunoglobulin having LPS binding site binding activity on alkaline phosphatase.

9. (amended) A method according to ~~any of the preceding claims~~ claim 1, wherein the LPS binding site binding ligand has at least the affinity for the LPS binding site of alkaline phosphatase of LPS

10. (amended) A method according to ~~any of the preceding claims~~ claim 1 wherein the LPS binding site binding ligand has at least the affinity for the LPS binding site of alkaline phosphatase of lipid A.

11. (amended) A method according to ~~any of claims 1-5~~ claim 1 wherein the degree of AP occupancy of LPS binding sites on alkaline phosphatase is determined by assessment of the dephosphorylating capacity of alkaline phosphatase in the sample.

14. (amended) A method according to ~~any of the preceding claims~~ claim 1 wherein the sample is from a cholestasis free patient.

15. (amended) A method according to ~~any of claims 1-13~~ claim 1 wherein the method also comprises a further assay of a sample from the patient for another

disease related to increase of alkaline phosphatase activity, said further assay employing a method avoiding determination of alkaline phosphatase level.

17. (amended) A method according to ~~any of claims 1-13~~ claim 1, wherein the sample is taken from an individual at risk of Gram negative bacterial infection.

19. (amended) A method according to ~~any of the preceding claims~~ claim 1 wherein the sample is taken from an individual during hospitalization.

20. (amended) A method according to ~~any of the preceding claims~~ claim 1 wherein the sample is taken a number of times over a period of time and the data are compared thus revealing the level of AP occupancy over time.

21. (amended) A method according to ~~any of the preceding claims~~ claim 1 wherein the period of time is as long as the individual is at risk of infection i.e. during hospitalization or post trauma recovery.

22. (amended) A method according to ~~any of the preceding claims~~ claim 1 wherein the result of the assay is compared to a standard value thus revealing whether the degree of AP occupancy is indicative of endotoxemia or sepsis or the risk thereof.

23. (amended) A method according to ~~any of the preceding claims~~ claim 1 wherein the sample is a sample selected from the group consisting of blood and tissue, said blood sample for example being serum, and the tissue being other than bone and said tissue for example being selected from liver and intestine.

24. (amended) A kit comprising alkaline phosphatase LPS binding site binding ligand and instructions for carrying out an assay according to ~~any of the preceding claims~~ claim 1 and any additional component required for such assay being selected from the following group of said group consisting of detectable marker, buffer, containers, comparative samples, data charts e.g. standard curves and data concerning relevant data of alkaline phosphatase values.

30. (amended) Use of a compound with an LPS binding site of alkaline phosphatase such as LPS, lipid A or a ligand which binds to the LPS binding site of AP as described in ~~any of the preceding claims~~ claim 1 as active compound in a method of preparation for medicament for therapy or diagnosis.

31. (amended) Use of a compound with an LPS binding site of alkaline phosphatase such as LPS, lipid A or a ligand which binds to the LPS binding site of AP as described in ~~any of the preceding claims~~ claim 1 as active compound in

a method of preparation for as medicament for therapy or diagnosis of endotoxemia or sepsis.

36. (amended) A method or use according to ~~any of the preceding claims~~ claim 1 wherein the method is carried out on a sample derived from the group of individuals consisting of a patient, an individual at risk of Gram negative bacterial infection, an individual prior to or after trauma, an individual during hospitalization.

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